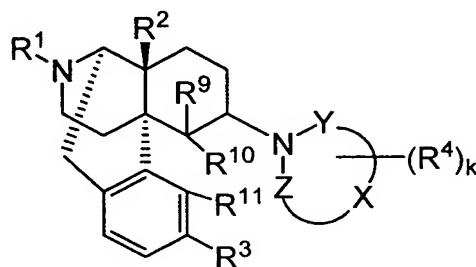


## CLAIMS

1. A therapeutic or prophylactic agent for urinary frequency or urinary incontinence, comprising as an effective ingredient a morphinan derivative having a nitrogen-containing heterocyclic group of the Formula (I):



(I)

[wherein  $R^1$  is hydrogen,  $C_1$ - $C_5$  alkyl,  $C_4$ - $C_7$  cycloalkylalkyl,  $C_6$ - $C_8$  cycloalkenylalkyl,  $C_6$ - $C_{12}$  aryl,  $C_7$ - $C_{13}$  aralkyl,  $C_3$ - $C_7$  alkenyl, furanylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5), thienylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5) or pyridylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5),  $R^2$  and  $R^3$  independently are hydrogen, hydroxy,  $C_1$ - $C_5$  alkoxy,  $C_3$ - $C_7$  alkenyloxy,  $C_7$ - $C_{13}$  aralkyloxy or  $C_1$ - $C_5$  alkanoyloxy; Y and Z independently represent valence bond or  $-C(=O)-$ ;  $-X-$  represents a  $C_2$ - $C_7$  carbon chain (one or more of the carbon atoms therein may be substituted by nitrogen, oxygen or sulfur atom(s), and the carbon chain may contain an unsaturated bond) constituting a part of the ring structure; k is an integer of 0 to 8;  $R^4$  is(are) (a) substituent(s) in the number of k on the nitrogen-containing ring, which independently represent(s) fluorine, chlorine, bromine, iodine, nitro, hydroxy,  $C_1$ - $C_5$  alkyl,  $C_7$ - $C_{13}$  cycloalkylalkyl,  $C_6$ - $C_{12}$  aryl,  $C_7$ - $C_{13}$  aralkyl,  $C_7$ - $C_{13}$  aralkyloxy,  $C_1$ - $C_5$  alkoxy, trifluoromethyl, trifluoromethoxy, cyano, isothiocyanato,  $SR^6$ ,  $SOR^6$ ,  $SO_2R^6$ ,  $(CH_2)_pOR^6$ ,  $(CH_2)_pCOR^6$ ,  $(CH_2)_pCO_2R^6$ ,  $SO_2NR^7R^8$ ,  $CONR^7R^8$ ,  $(CH_2)_pNR^7R^8$  or  $(CH_2)_pN(R^7)COR^8$ , or among the  $R^4$ s in the number of k, two  $R^4$ s bound to the same carbon atom or to the same sulfur atom cooperatively represent one oxygen

atom to form carbonyl or sulfoxide, or two  $R^4$ 's bound to the same carbon atom cooperatively represent one sulfur atom to form thiocarbonyl, or four  $R^4$ 's bound to the same sulfur atom cooperatively represent two oxygen atoms to form sulfone, or among the  $R^4$ 's in the number of k, two  $R^4$ 's bound to adjacent carbon atoms, respectively, cooperatively form benzene condensed ring, pyridine condensed ring, naphthalene condensed ring, cyclopropane fused ring, cyclobutane fused ring, cyclopentane fused ring, cyclopentene fused ring, cyclohexane fused ring, cyclohexene fused ring, cycloheptane fused ring or cycloheptene fused ring, each of said fused rings is non-substituted or substituted by 1 or more  $R^5$ 's, wherein  $R^5$ (s) independently represent(s) fluorine, chlorine, bromine, iodine, nitro, hydroxy,  $C_1$ - $C_5$  alkyl,  $C_1$ - $C_5$  alkoxy, trifluoromethyl, trifluoromethoxy, cyano,  $C_6$ - $C_{12}$  aryl, isothiocyanato,  $SR^6$ ,  $SOR^6$ ,  $SO_2R^6$ ,  $(CH_2)_pOR^6$ ,  $(CH_2)_pCOR^6$ ,  $(CH_2)_pCO_2R^6$ ,  $SO_2NR^7R^8$ ,  $CONR^7R^8$ ,  $(CH_2)_pNR^7R^8$  or  $(CH_2)_pN(R^7)COR^8$ ;  $R^9$  is hydrogen,  $C_1$ - $C_5$  alkyl,  $C_1$ - $C_5$  alkenyl,  $C_7$ - $C_{13}$  aralkyl,  $C_1$ - $C_3$  hydroxyalkyl,  $(CH_2)_pOR^6$  or  $(CH_2)_pCO_2R^6$ ;  $R^{10}$  and  $R^{11}$  are bound to form -O-, -S- or -CH<sub>2</sub>-, or  $R^{10}$  is hydrogen and  $R^{11}$  is hydrogen, hydroxy,  $C_1$ - $C_5$  alkoxy or  $C_1$ - $C_5$  alkanoyloxy; p is an integer of 0 to 5;  $R^6$  is hydrogen,  $C_1$ - $C_5$  alkyl,  $C_3$ - $C_7$  alkenyl,  $C_6$ - $C_{12}$  aryl or  $C_7$ - $C_{13}$  aralkyl; and  $R^7$  and  $R^8$  independently are hydrogen,  $C_1$ - $C_5$  alkyl or  $C_7$ - $C_{13}$  aralkyl] or a pharmaceutically acceptable acid addition salt thereof.

2. The therapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 1, wherein in said Formula (I), only one of Y and Z is -C(=O)- and the other is valence bond.

3. The therapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 1, wherein in said Formula (I), both Y and Z are -C(=O)-.

4. The therapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 3, wherein in said Formula (I),  $R^1$  is hydrogen,  $C_4$ -

C<sub>7</sub> cycloalkylalkyl, C<sub>6</sub>-C<sub>8</sub> cycloalkenylalkyl, C<sub>6</sub>-C<sub>12</sub> aryl or C<sub>3</sub>-C<sub>7</sub> alkenyl; and two R<sup>4</sup>s bound to adjacent carbon atoms, respectively, cooperatively form benzene fused ring, pyridine fused ring, naphthalene fused ring, cyclopropane fused ring, cyclobutane fused ring, cyclopentane fused ring, cyclopentene fused ring, cyclohexane fused ring, cyclohexene fused ring, cycloheptane fused ring or cycloheptene fused ring, each of said fused rings is non-substituted or substituted by 1 or more R<sup>5</sup>s.

5. The therapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 3, wherein in said Formula (I), R<sup>1</sup> is hydrogen, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, allyl or prenyl; R<sup>2</sup> is hydrogen, hydroxy, methoxy, ethoxy, allyloxy, benzyloxy, acetoxy or propionoxy; R<sup>3</sup> is hydrogen, hydroxy, methoxy, ethoxy, benzyloxy, acetoxy or propionoxy; k is an integer of 0 to 6, two R<sup>4</sup>s cooperatively form benzene fused ring which is non-substituted or substituted by 1 to 4 R<sup>5</sup>s; R<sup>5</sup>(s) independently is(are) fluorine, chlorine, bromine, iodine, nitro, methyl, ethyl, propyl, benzyl, hydroxy, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, cyano, phenyl, isothiocyanato, SR<sup>6</sup>, SOR<sup>6</sup>, SO<sub>2</sub>R<sup>6</sup>, (CH<sub>2</sub>)<sub>p</sub>OR<sup>6</sup>, (CH<sub>2</sub>)<sub>p</sub>COR<sup>6</sup>, (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>6</sup>, SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, CONR<sup>7</sup>R<sup>8</sup>, (CH<sub>2</sub>)<sub>p</sub>NR<sup>7</sup>R<sup>8</sup> or (CH<sub>2</sub>)<sub>p</sub>N(R<sup>7</sup>)COR<sup>8</sup>; p is an integer of 0 to 5; R<sup>6</sup> is hydrogen, methyl, ethyl, propyl or phenyl; R<sup>7</sup> and R<sup>8</sup> independently are hydrogen, methyl, ethyl, propyl or benzyl; R<sup>9</sup> is hydrogen or methyl; R<sup>10</sup> and R<sup>11</sup> are bound to form -O-, or R<sup>10</sup> is hydrogen and R<sup>11</sup> is hydrogen, hydroxy or methoxy.

6. The therapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 1, wherein in said Formula (I), both Y and Z are valence bonds.

7. The therapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 6, wherein in said Formula (I), R<sup>1</sup> is hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>7</sub>-C<sub>13</sub> aralkyl, furanylalkyl (wherein the number of carbon atoms in the

alkyl moiety is 1 to 5), thienylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5) or pyridylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5); two  $R^4$ s bound to adjacent carbon atoms, respectively, cooperatively form benzene fused ring, pyridine fused ring, naphthalene fused ring, cyclopropane fused ring, cyclobutane fused ring, cyclopentane fused ring, cyclopentene fused ring, cyclohexane fused ring, cyclohexene fused ring, cycloheptane fused ring or cycloheptene fused ring, each of said fused rings is non-substituted or substituted by 1 or more  $R^5$ s.

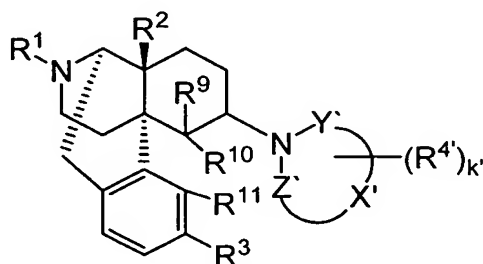
8. Thetherapeutic or prophylactic agent for urinary frequency or urinary incontinence according to claim 6, wherein in said Formula (I),  $R^1$  is hydrogen, methyl, ethyl, propyl, benzyl, phenethyl, phenylpropyl, 2-furanylmethyl, 2-furanylethyl, 2-furanylpropyl, 3-furanylmethyl, 3-furanylethyl, 3-furanylpropyl, 2-thiophenylmethyl, 2-thiophenylethyl, 2-thiophenylpropyl, 3-thiophenylmethyl, 3-thiophenylethyl, 3-thiophenylpropyl, 2-pyridynylmethyl, 2-pyridynylethyl, 2-pyridynylpropyl, 3-pyridynylmethyl, 3-pyridynylethyl, 3-pyridynylpropyl, 4-pyridynylmethyl, 4-pyridynylethyl, or 4-pyridynylpropyl;  $R^2$  is hydrogen, hydroxy, methoxy, ethoxy, allyloxy, benzyloxy, acetoxy or propionoxy;  $R^3$  is hydrogen, hydroxy, methoxy, ethoxy, benzyloxy, acetoxy or propionoxy; k is an integer of 0 to 6; two  $R^4$ s cooperatively form benzene fused ring which is non-substituted or substituted by 1 to 4  $R^5$ s and other  $R^4$ (s) independently is(are) methyl, ethyl, propyl or benzyl, or two  $R^4$ s bound to the same carbon atom represent one oxygen atom to form carbonyl,  $R^5$ (s) independently is(are) fluorine, chlorine, bromine, iodine, nitro, methyl, ethyl, propyl, benzyl, hydroxy, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, cyano, phenyl, isothiocyanato,  $SR^6$ ,  $SOR^6$ ,  $SO_2R^6$ ,  $(CH_2)_pOR^6$ ,  $(CH_2)_pCOR^6$ ,  $(CH_2)_pCO_2R^6$ ,  $SO_2NR^7R^8$ ,  $CONR^7R^8$ ,  $(CH_2)_pNR^7R^8$  or  $(CH_2)_pN(R^7)COR^8$ ; p is an integer of 0 to 5;  $R^6$  is hydrogen, methyl, ethyl, propyl or phenyl;  $R^7$  and  $R^8$  independently are hydrogen, methyl, ethyl, propyl or benzyl;  $R^9$  is

hydrogen or methyl;  $R^{10}$  and  $R^{11}$  are bound to form -O-, or  $R^{10}$  is hydrogen and  $R^{11}$  is hydrogen, hydroxy or methoxy.

9. A method for therapy or prophylaxis for urinary frequency, urinary urgency or urinary incontinence, comprising using said morphinan derivative having a nitrogen-containing heterocyclic group according to any one of claims 1 to 8, or a pharmaceutically acceptable acid addition salt thereof.

10. Use of said morphinan derivative having a nitrogen-containing heterocyclic group according to any one of claims 1 to 8, or a pharmaceutically acceptable acid addition salt thereof for urinary frequency, urinary urgency or urinary incontinence.

11. A morphinan derivative of the Formula (II) having a nitrogen-containing heterocyclic group:



( II )

[wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^9$ ,  $R^{10}$  and  $R^{11}$  represent the same meanings as described above,  $R^4$ ,  $X'$ ,  $Y'$ ,  $Z'$  and  $k'$  represent the same meanings as said  $R^4$ ,  $X$ ,  $Y$ ,  $Z$  and  $k$  with the proviso that in cases where  $Y'$  and  $Z'$  are simultaneously valence bonds and  $X'$  is  $-(CH_2)_4-$ ,  $-(CH_2)_5-$  or  $-(CH_2)_2-O-(CH_2)_2-$ ,  $k'$  must be not less than 1, in cases where  $Y'$  and  $Z'$  are simultaneously  $-C(=O)-$  and  $X'$  is a chain comprising two carbon atoms constituting the ring structure,  $k'$  must be not less than 1, and in particular, in cases where  $(R^4)_{k'}$  is a benzene fused ring, the benzene ring must be substituted by the  $R^5$ ]

or a pharmaceutically acceptable acid addition salt thereof.

12. The morphinan derivative or the pharmaceutically acceptable acid addition

salt thereof according to claim 11, wherein in said Formula (II), only one of Y' and Z' is -C(=O)- and the other is valence bond.

13. The morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to claim 11, wherein in said Formula (II), both Y' and Z' are -C(=O)-.

14. The morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to claim 13, wherein in said Formula (II), R<sup>1</sup> is hydrogen, C<sub>4</sub>-C<sub>7</sub> cycloalkylalkyl, C<sub>6</sub>-C<sub>8</sub> cycloalkenylalkyl, C<sub>6</sub>-C<sub>12</sub> aryl or C<sub>3</sub>-C<sub>7</sub> alkenyl; and two R<sup>4'</sup>s bound to adjacent carbon atoms, respectively, cooperatively form benzene fused ring, pyridine fused ring, naphthalene fused ring, cyclopropane fused ring, cyclobutane fused ring, cyclopentane fused ring, cyclopentene fused ring, cyclohexane fused ring, cyclohexene fused ring, cycloheptane fused ring or cycloheptene fused ring, each of said fused rings is non-substituted or substituted by 1 or more R<sup>5</sup>s.

15. The morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to claim 13, wherein in said Formula (II), R<sup>1</sup> is hydrogen, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, allyl or prenyl; R<sup>2</sup> is hydrogen, hydroxy, methoxy, ethoxy, allyloxy, benzyloxy, acetoxy or propionoxy; R<sup>3</sup> is hydrogen, hydroxy, methoxy, ethoxy, benzyloxy, acetoxy or propionoxy; k' is an integer of 0 to 6, two R<sup>4'</sup>s cooperatively form benzene fused ring which is non-substituted or substituted by 1 to 4 R<sup>5</sup>s; R<sup>5</sup>(s) independently is(are) fluorine, chlorine, bromine, iodine, nitro, methyl, ethyl, propyl, benzyl, hydroxy, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, cyano, phenyl, isothiocyanato, SR<sup>6</sup>, SOR<sup>6</sup>, SO<sub>2</sub>R<sup>6</sup>, (CH<sub>2</sub>)<sub>p</sub>OR<sup>6</sup>, (CH<sub>2</sub>)<sub>p</sub>COR<sup>6</sup>, (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>6</sup>, SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, CONR<sup>7</sup>R<sup>8</sup>, (CH<sub>2</sub>)<sub>p</sub>NR<sup>7</sup>R<sup>8</sup> or (CH<sub>2</sub>)<sub>p</sub>N(R<sup>7</sup>)COR<sup>8</sup>; p is an integer of 0 to 5; R<sup>6</sup> is hydrogen, methyl, ethyl, propyl or phenyl; R<sup>7</sup> and R<sup>8</sup> independently are hydrogen, methyl, ethyl, propyl or benzyl; R<sup>9</sup> is hydrogen or methyl; R<sup>10</sup> and R<sup>11</sup> are bound to form -O-, or R<sup>10</sup> is

hydrogen and  $R^{11}$  is hydrogen, hydroxy or methoxy.

16. The morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to claim 11, wherein in said Formula (II), both  $Y'$  and  $Z'$  are valence bonds.

5 17. The morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to claim 16, wherein in said Formula (II),  $R^1$  is hydrogen,  $C_1-C_5$  alkyl,  $C_7-C_{13}$  aralkyl, furanylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5), thienylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5) or pyridylalkyl (wherein the number of carbon atoms in the alkyl moiety is 1 to 5); two  $R^{4'}$ 's bound to adjacent carbon atoms, respectively,  
10 cooperatively form benzene fused ring, pyridine fused ring, naphthalene fused ring, cyclopropane fused ring, cyclobutane fused ring, cyclopentane fused ring, cyclopentene fused ring, cyclohexane fused ring, cyclohexene fused ring, cycloheptane fused ring or cycloheptene fused ring, each of said fused rings is non-  
15 substituted or substituted by 1 or more  $R^5$ 's.

18. The morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to claim 16, wherein in said Formula (II),  $R^1$  is hydrogen, methyl, ethyl, propyl, benzyl, phenethyl, phenylpropyl, 2-furanylmethyl, 2-furanylethyl, 2-furanylpropyl, 3-furanylmethyl, 3-furanylethyl, 3-furanylpropyl, 2-thiophenylmethyl, 2-thiophenylethyl, 2-thiophenylpropyl, 3-thiophenylmethyl, 3-thiophenylethyl, 3-thiophenylpropyl, 2-pyridynylmethyl, 2-pyridynylethyl, 2-pyridynylpropyl, 3-pyridynylmethyl, 3-pyridynylethyl, 3-pyridynylpropyl, 4-pyridynylmethyl, 4-pyridynylethyl, or 4-pyridynylpropyl;  $R^2$  is hydrogen, hydroxy, methoxy, ethoxy, allyloxy, benzyloxy, acetoxy or propionoxy;  $R^3$  is hydrogen, hydroxy, methoxy, ethoxy, benzyloxy, acetoxy or propionoxy;  $k'$  is an integer of 0 to  
20 6; two  $R^{4'}$ 's cooperatively form benzene fused ring which is non-substituted or substituted by 1 to 4  $R^5$ 's and other  $R^{4'}$ (s) independently is(are) methyl, ethyl, propyl

or benzyl, or two  $R^{4'}$ 's bound to the same carbon atom represent one oxygen atom to form carbonyl,  $R^5$ (s) independently is(are) fluorine, chlorine, bromine, iodine, nitro, methyl, ethyl, propyl, benzyl, hydroxy, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, cyano, phenyl, isothiocyanato,  $SR^6$ ,  $SOR^6$ ,  $SO_2R^6$ ,  $(CH_2)_pOR^6$ ,  $(CH_2)_pCOR^6$ ,  $(CH_2)_pCO_2R^6$ ,  $SO_2NR^7R^8$ ,  $CONR^7R^8$ ,  $(CH_2)_pNR^7R^8$  or  $(CH_2)_pN(R^7)COR^8$ ; p is an integer of 0 to 5;  $R^6$  is hydrogen, methyl, ethyl, propyl or phenyl;  $R^7$  and  $R^8$  independently are hydrogen, methyl, ethyl, propyl or benzyl;  $R^9$  is hydrogen or methyl;  $R^{10}$  and  $R^{11}$  are bound to form -O-, or  $R^{10}$  is hydrogen and  $R^{11}$  is hydrogen, hydroxy or methoxy.

10 19. A pharmaceutical comprising the morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to any one of claims 11 to 18.

20. A pharmaceutical composition comprising the morphinan derivative or the pharmaceutically acceptable acid addition salt thereof according to any one of claims 15 11 to 18.